The Professional Medical Journal
www.theprofesional.com

DOI: 10.29309/TPMJ/18.4572

ORIGINAL PROF-4572

DIABETIC RETINOPATHY;

CENTRAL MACULAR THICKNESS IN DIABETIC RETINOPATHY IN PATIENTS PRESENTING AT A TERTIARY CARE HOSPITAL.

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Article received on:
23/10/2017
Accepted for publication:
10/03/2018
Received after proof reading:
02/06/2018

ABSTRACT… Objectives: To determine central macular thickness (CMT) in Diabetic retinopathy (DR) in type 2 diabetic subjects. **Study Design:** Cross sectional comparative study. **Place & Duration:** Department of Ophthalmology, Al- Ibrahim Eye Hospital & Al-Tibri Medical College, Karachi from June 2014 to May 2015. **Subjects & Methods:** A sample of 200 diabetics was examined. Ophthalmological examination was performed and included the best corrected visual acuity (BCVA), anterior and posterior segment examination was performed. A +90 dioptre lens was used for the anterior and posterior segment examination. Optical coherence tomography (OCT) was used with Zeiss Cirrus HD– OCT 500. Central macular thickness (CMT) was defined as an average 1 millimeter CMT. Three reading of CMT were taken and average of three was calculated. Data was analyzed on SPSS 23.0 ver at 95% confidence interval (P value <0.05). **Results:** Mean age was found 50.53± 13.75 years. Of 200 study subjects 150 (75%) were male and 50 (25%) were female (M: F ratio 3:1). Hemoglobin A1c was noted as 9.78±3.31. Central macular thickness (CMT) in HbA1c <7.0% and >7.0% was noted as 521.73±33.50 and 348.47± 34.33 μm respectively (P=0.0001). **Conclusion:** Diabetics with retinopathy must be followed up frequently to examine for central macular thickness to prevent visual loss. Optical coherence tomography is best available technique to detect the central macular thickness.

Key words: Central Macular Thickness, Diabetic Retinopathy, Optical Coherence Tomography, Visual Loss.

Article Citation: Jamali KK, Channa S, Azam M. Diabetic retinopathy; central macular thickness in diabetic retinopathy in patients presenting at a tertiary care hospital. Professional Med J 2018; 25(6):947-951.
DOI:10.29309/TPMJ/18.4572

INTRODUCTION

Diabetes mellitus (DM) is the most common chronic metabolic disorder. It is characterized by chronic hyperglycemia caused by relative or absolute insulin deficiency. DM affects the micro and microvasculature of every organ of body. Micro vascular complications put the patients at high risk of morbidity and mortality. Common clinical symptoms of DM are the polyuria, polydipsia, polyphagia, numbness, and paresthesia, etc. DM is a long ongoing health problem which damages organs and nerves.[1,2] Microvascular complications include the nephropathy, neuropathy, retinopathy, and microvascular angiopahty. By far the diabetic retinopathy (DR) is the most notorious complication.[3,4] Diabetic retinopathy (DR) has become noticeable cause of blindness in diabetic subjects. It now accounts for a large number of blindness in adult population. Macular edema (ME) is a sign of DR which almost always progresses to complete blindness. Early diagnosis and intervention may halt the disease process and prevention of blindness.[5] Glycemic control and timely intervention must be initiated to prevent complications of DR and postpones the disease process and potential visual compromise. Approximately 10% diabetics are suffering from ME. Prevalence of DR is high in type 2 DM compared to type 1 DM subjects. Major factors which control the visual acuity in ME of DR are the; central fovea involvement, peri-foveal capillary congestion, peri- foveal capillary occlusion, retinal thickness, and central macular thickness (CMT). Optical coherence tomography (OCT) is a new non-invasive imaging modality used to diagnose and treat macular disease.[6] OCT shows strong predictive correlation significance between central fovea thickness and visual acuity. OCT is now a clinical test used by the ophthalmologists. OCT diagnoses the macular

thickness in diabetics with ME. Sub clinical macular thickening can be detected by OCT for ME in Diabetic Retinopathy.[7] Despite wide clinical use of OCT, there is limited published literature on the retina and macula thickness in DR. Measuring retinal and macular thickness in DR is necessary to diagnose the pathological changes in diabetic population. Previous studies have produced conflicting results on the CMT in DR using OCT; variable findings have been reported.[8,9] Some studies[10,11] reported thin peri- central macular thickness in stage 1 DR patients. Theoretically, it is justified by the hypothesis that the neuronal loss does occur during early stages of DR which causes significant thinning in macula. Contrary to this, other studies reported that the diabetics with DR have thick retina and macula; approximately >40 µm in diabetics compared to the non-diabetic controls.[11,12] Visual acuity depends on healthy central macula which is the most sensitive part of retina. Underlying pathological mechanism of ME is the occlusion and collapse of inner blood-retina barrier causes outpouring, seepage and collection of exudates within the retina resulting in macular edema. Edema of macula results in diminished visual acuity in diabetic retinopathy. Evaluating the central macular thickness (CMT) is highly significant in diabetics to prevent blindness.[11,12] Current medical literatures on the central macular thickness have lacunae, and there is need to collect more data on the CMT in diabetic retinopathy. The present study was conducted to assess the changes in the central macular thickness in diabetic retinopathy in type 2 diabetics.

Subjects and Methods

The present comparative observational study was conducted at the Department of Ophthalmology, Al- Ibrahim Eye Hospital & Al-Tibri Medical College Karachi from June 2014 to May 2015. A sample of 200 diabetics was selected and divided into Group A (n=100) - HbA1c <7.0% and Group B (n=100) - HbA1c >7.0%. Diabetes mellitus was defined as per American Diabetes Association criteria of Random Blood Glucose ≥200 mg/dl, or Fasting Blood Glucose > 126 mg/dl.[13] Subjects were communicated during interview session about the purpose of study, benefits and loss to them. They were informed that the study is on volunteer basis. They don't have to spend any expenses if participate. Volunteers were selected who gave a writing consent. Participants were informed that they are not bound and can withdraw at any time if feeling worrisome, anxious, or without telling the reason. Antecubital vein was marked and washed with sterile alcohol swab for venepuncture. 5 ml blood was taken and processed for the glycated HbA1 (HbA1c), blood glucose and cholesterol estimation. Each case was examined of Macula for the Clinically Significant Macular Edema (CSME) as present or absent. Exclusion criteria were a co-existing macular pathology, a history of retinal laser therapy and history of ophthalmological surgery.

Diabetic retinopathy was graded according to the International Clinical Diabetic Retinopathy Disease Severity Scale (ICDRDSS).[13] Stage 1- was defined as a diabetic having no apparent retinopathy, Stage 2- having mild non-proliferative retinopathy, Stage 3- having moderate non-proliferative retinopathy, Stage 4- having severe non-proliferative retinopathy, and Stage 5- as Diabetics with Proliferative Diabetic Retinopathy (PDR).

Demographic data of study subjects was recorded as per protocol on predesigned proforma. Ophthalmological examination was performed and included the best corrected visual acuity (BCVA), anterior and posterior segment examination was performed. A +90 dioptre lens was used for the anterior and posterior segment examination. Optical coherence tomography (OCT) was used with Zeiss Cirrus HD– OCT 500. 2.5% Phenylephrine HCl and 1% tropicamide were used for the pupil dilation. Macula was examined after pupils were full dilated. Topographical map of macula generated by OCT which was interpreted as per guidelines of the Early Treatment of Diabetic Retinopathy Study (ETDRS). Central macular thickness (CMT) was defined as an average 1 millimeter CMT. Three reading of CMT were taken and average of three was calculated. Data was analyzed on SPSS 23.0 ver for windows (IBM, Incorporation, USA). One sample and independent sample Student's t-test

were used for the analysis of age, BMI, blood pressure, and the central macular thickness respectively. Frequency of severity of Diabetic retinopathy was analysed by the Chi-square test. Data was analysed at 95% confidence interval (P value <0.05).

RESULTS

Mean± SD age was found 50.53± 13.75 years. Of 200 study subjects 150 (75%) were male and 50 (25%) were female. Male to female ratio was 3:1. BMI, Systolic and Diastolic BP, Blood Glucose and Cholesterol are summarized in Table-I. Blood pressure, blood glucose and cholesterol were elevated in study subjects. Hemoglobin A1c was noted as 9.78±3.31. Central macular thickness (CMT) in HbA1c <7.0% and >7.0% was noted as 521.73±33.50 and 348.47± 34.33 μm respectively (P=0.0001). CMT is shown in Table-II and Figure-1. Staging of Diabetic retinopathy is shown in Table-III and Figure-2.

	Mean	SD
Age	50.53	13.75
BMI (kg/m^2)	27.42	9.81
Systolic BP (mmHg)	145.53	29.53
Diastolic BP (mmHg)	91.57	13.52
Blood glucose (mg/dl)	209.53	56.51
Cholesterol (mg/dl)	217.50	47.91
HbA1c (%)	9.78	3.31

Table-I. Characteristics of study population (n=200)

	Mean	SD	P-value
Group A. (HbA1c (>7.0%)	521.73	33.50	0.0001
Group B. HbA1c (<7.0%)	348.47	34.33	

Table-II. Central macular thickness (CMT) (μm) (n=200)

Staging	HbA1c (<7.0%)	HbA1c (>7.0%)	P-value
Stage 1	53	43	0.0001
Stage 2	13	15	
Stage 3	24	27	
Stage 4	7	7	
Stage 5	3	8	

Table-III. Frequency of severity of Diabetic retinopathy

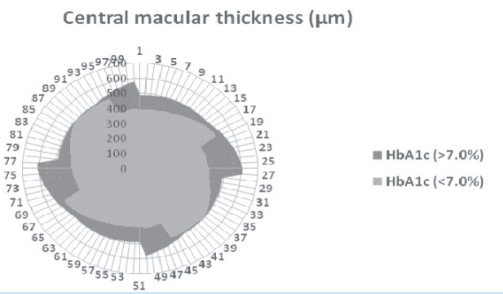

Figure-1. Central macular thickness according to HbA1c

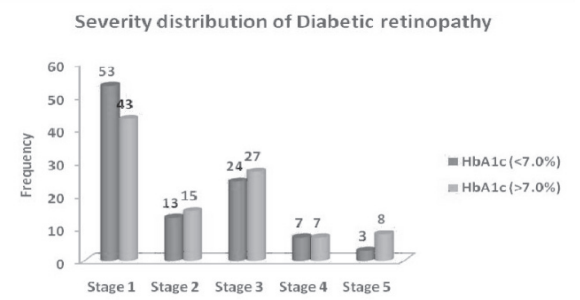

Figure-2. Frquency distribution of Diabetic retinopahty according to stage

In present study the mean± SD age was found 50.53± 13.75 years. Of 200 study subjects 150 (75%) were male and 50 (25%) were female. Male to female ratio was 3:1. These findings are in keeping with previous studies.[1,5,14-16] which have reported similar results. Mean± SD hemoglobin A1c was noted as 9.78±3.31. Also the Central macular thickness (CMT) was noted as 521.73±33.50 in HbA1c <7.0% and >7.0% and 348.47± 34.33 μm respectively (P=0.0001). (Table-II and Figure-1). The CMT revealed direct proportion to glycemic control of DM (Table-III and Figure-2).

DISCUSSION

DM is major health problem of World. Approximately 371 million people are suffering from diabetes in the World. And an equal number of diabetics are undiagnosed, unnoticed and under reported; hence the toll may be high than the current estimates.[14] Approximate prevalence of DM and DR is reported as 10% and 27% respectively in Pakistan.[15] DR is notorious for it causes visual loss and ocular blindness among diabetics.[16] The findings are supported by previous studies. Abrar et al[5] reported CMT of 291.0±63.0 μm in diabetic retinopathy. Results of present study show the CMT was very high in

our study subjects this may be because of bad glycemic control in our diabetic population. It is stated that the retinal capillary become leaky and lipid exudates accumulates within the layers of retina causing macular edema and increased CMT. This is major cause of ocular loss in DR in the diabetic subjects; hence assessment of retina and macula should be screened timely. Optical coherence tomography (OCT) quantifies the thickness of macula for proper diagnosis and treatment of DR.[17] Previous studies[18,19] suggested that the hyperglycemia changes permeability of retinal capillary, damages the blood-retina barrier, this causes exudation of plasma proteins and lipids and micro hemorrhages, these together increase the CMT.

Other researchers[20,21] reported that the macular thickening is noted earlier that retinopathy; however these studies produced non- significant conclusions. The results of present study are in agreement with previous studies.[1,5,22] Oshitari et al[22] reported the pathogenesis of central macula occurs during early stages of DR. Central macular thickness was thicker than control subjects in their study.[22] Reason was loss of retinal ganglion in diabetics with axonal degeneration. They concluded that the vascular abnormalities occur at early stage before the retinopathy becomes clinically evident. In present study, the mean CMT shows progressive increase with increasing stage of DR. Our findings are in agreement with previous studies.[23,24] Thick macula occurs due to change in retinal vessel permeability in foveal and macula areas with exudation of plasma proteins, lipids, etc in diabetic eyes.

The present study shows increasing stages of CMT in DR and statistically significant differences with noted when comparing PDR and NPDR and mild, moderate and severe PDR ($P < 0.05$) as shown in Table-II. Our findings are in keeping with previous study.[25] Stage 5 shows severe increase in CMT compared to other stages ($P = 0.0001$). This in keeping with previous study[26] and is justified by the fact of increased vascular micro-aneurysms and plasma exudation within the macular area. The present study suggests the OCT is best approach to detect the macular thickness in diabetics despite normal findings. The diabetics with macular thickness must be followed for retinal examination frequently for timely intervention to prevent visual loss.

CONCLUSION

The present study reports increasing macular thickness with increasing stages of diabetic retinopathy and bad glycemic control. Diabetics with retinopathy must be followed up frequently to examine for central macular thickness to prevent visual loss. Optical coherence tomography is best available technique to detect the central macular thickness.

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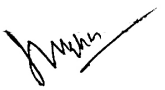
AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Khamiso Khan Jamali	Literature review, manuscript writing, data collection, Research Proposal, Concept, Study design.	
2	Shahnawaz Channa	Data collection, data analysis, Tabulation, graphing, manuscript write, Data interpretation, Final review, Critical review, amendments.	
3	Muhammad Azam	Data collection and analysis, manuscript writing.